

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

21-449

CHEMISTRY REVIEW(S)



NDA 21-449

Adefovir Dipivoxil

Gilead Science , Inc.

Ko-Yu Lo, Ph.D.
Division of Antiviral Drug Products

Chemistry Review Data Sheet

1. NDA # 21-449
2. REVIEW # 1
3. REVIEW DATE: 9/17/2002
4. REVIEWER: Ko-Yu Lo, Ph.D.
5. PREVIOUS DOCUMENTS:

Previous Documents
N/A

Document Date

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed

Document Date

Original
Amendment BZ
Amendment BL
Amendment BL
Amendment BZ
Amendment
Amendment BC

21/MAR/2002
29/MAY/2002
12/JUN/2002
19/AUG/2002
23/AUG/2002
29/AUG/2002
11/SEP/2002

7. NAME & ADDRESS OF APPLICANT:

Name: Gilead Sciences, Inc.



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Address: 333 Lakeside Drive
Foster City, CA 94404

Representative: Martine Kraus, Ph.D.

Telephone: 650-522-5722

8. DRUG PRODUCT NAME/CODE/TYPE:

- a) Proprietary Name: HEPSERA™
- b) Non-Proprietary Name (USAN): Adefovir Dipivoxil
- c) Code Name/# (ONDC only): GS-0840
- d) Chem. Type/Submission Priority (ONDC only):
 - Chem. Type: 1
 - Submission Priority: P

9. LEGAL BASIS FOR SUBMISSION: N/A

10. PHARMACOL. CATEGORY: Antiviral

11. DOSAGE FORM: Tablet

12. STRENGTH/POTENCY: 10 mg

13. ROUTE OF ADMINISTRATION: Oral

14. Rx/OTC DISPENSED: ☒ Rx ☐ OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM)[Note27]:

☐ SPOTS product – Form Completed

☒ Not a SPOTS product



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16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

9-[2-[[bis[(pivaloyloxy)methoxy]phosphinyl]methoxy]ethyl]adenine (IUPAC)
Propanoic acid, 2,2-dimethyl-, [[[[2-(6-amino-9H-purine-9-yl)ethoxy]methyl]-phosphinylidene]bis(oxymethylene)ester (CAS)

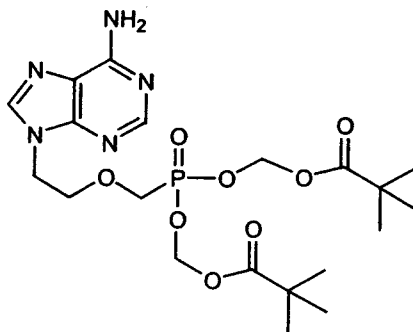
CAS Reg. No. 142340-99-6

Synonym: bis-POM PMEA

Molecular formula $C_{20}H_{32}N_5O_8P$

Molecular weight 501.48

Structure formula



17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE ¹	STATUS ²	DATE REVIEW COMPLETED	COMMENTS
1	III			4	N/A		
2	III			3	Adequate	12/15/1999	
3	III			4	N/A		
4	III			4	N/A		
5	III			3	Adequate	3/2/2000	



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	III					10/30/2001
				3	Adequate	2/28/2000
				7	Adequate	
	III			3	Adequate	5/11/2000
	III			3	Adequate	9/10/1997
	III			3	Adequate	10/4/2001
	III			3	Adequate	4/13/2000
	III				Adequate	1/12/2001
	III			4	N/A	

¹ Action codes for DMF Table:

1 – DMF Reviewed.

Other codes indicate why the DMF was not reviewed, as follows:

2 – Type 1 DMF

3 – Reviewed previously and no revision since last review

4 – Sufficient information in application

5 – Authority to reference not granted

6 – DMF not available

7 – Other (explain under "Comments")

² Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
IND		Adefovir Dipivoxil
IND		Adefovir Dipivoxil
NDA		Adefovir Dipivoxil Tablets (30, 60 & 120 mg)



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18. STATUS:

CONSULTS/ EMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Biometrics	N/A		
EES	Acceptable	9/9/2002	(HFD-322)
Pharm/Tox	Impurity levels qualification adequate	9/9/2002	Peter Verma
Biopharm	Dissolution specification acceptable	9/9/2002	Robert Kumi
LNC	N/A		
Methods Validation	Pending		
OPDRA	Acceptable		
EA	Exclusion Acceptable		
Microbiology	N/A		

APPEARS THIS WAY
ON ORIGINAL

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Ko-yu Lo
9/23/02 12:41:23 PM
CHEMIST

Stephen Paul Miller
9/23/02 12:51:30 PM
CHEMIST

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

Application: NDA 21449/000	Priority: P	Org Code: 530
Stamp: 21-MAR-2002 Regulatory Due: 21-SEP-2002	Action Goal:	District Goal: 23-JUL-2002
Applicant: GILEAD	Brand Name:	(ADEFOVIR DIPIVOXIL)
333 LAKESIDE DR		10MG TABLETS
FOSTER CITY, CA 94404	Established Name:	
	Generic Name:	ADEFOVIR DIPIVOXIL
	Dosage Form:	TAB (TABLET)
	Strength:	10 MG
FDA Contacts: M. HOLLOMAN (HFD-530)	301-827-2335	, Project Manager
K. LO (HFD-530)	301-827-2397	, Review Chemist
S. MILLER (HFD-530)	301-827-2392	, Team Leader

Overall Recommendation:

ACCEPTABLE on 09-SEP-2002 by J. D AMBROGIO (HFD-324) 301-827-0062

Establishment: 2952384
GILEAD SCIENCES INC
346 LAKESIDE DR
FOSTER CITY, CA 94404

DMF No:
AADA No:

Profile: CTL OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 09-SEP-2002
Decision: ACCEPTABLE
Reason: DISTRICT RECOMMENDATION

Responsibilities: DRUG SUBSTANCE RELEASE
TESTER
FINISHED DOSAGE RELEASE
TESTER
FINISHED DOSAGE STABILITY
TESTER

Establishment:

DMF No:
AADA No:

Profile: CTL OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 03-MAY-2002
Decision: ACCEPTABLE
Reason: BASED ON PROFILE

Responsibilities:

Establishment:

DMF No:
AADA No:

Profile: TCM OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 08-MAY-2002

Responsibilities:

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**

Establishment: DMF No:
AADA No:

Profile: **CTL** OAI Status: **NONE** Responsibilities:
Last Milestone: **OC RECOMMENDATION**
Milestone Date: **06-MAY-2002**
Decision: **ACCEPTABLE**
Reason: **BASED ON PROFILE**

Establishment: DMF No:
AADA No:

Profile: **CSN** OAI Status: **NONE** Responsibilities:
Last Milestone: **OC RECOMMENDATION**
Milestone Date: **04-SEP-2002**
Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**

Establishment: DMF No:
AADA No:

Profile: **CSN** OAI Status: **NONE** Responsibilities:
Last Milestone: **OC RECOMMENDATION**
Milestone Date: **08-MAY-2002**
Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**
